## I. REMARKS

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claim 1 has been amended. Support for the amendment can be found at least in paragraph [0043]. After amending the claims as set forth above, claims 1-7 and 10-14 will be pending in this application.

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

## II. REJECTIONS UNDER 35 U.S.C. § 103

The examiner continues to reject the claims under 35 U.S.C. §103(a) as being upatentable over on Lee et al. in view of Blazquez et al., Chee et al. (A) (WO 95/11995) and Sutcliffe; and in further view of Osano et al.; and over Lee et al. in view of Blazquez et al., Chee et al. (A) (WO 95/11995) and Sutcliffe and in further view of Chee et al. (B) and Routier; and over Lee et al. in view of Blazquez et al., Chee et al. (A) (WO 95/11995) and Sutcliffe and in further view of Behrensdor. Applicants respectfully traverse the rejections.

The present methods and kits involve microarrays with capture probes utilizing the 44 triplets provided in table 1 and their mutant counterparts for the specific detection of the beta-lactamases TEM, ESBL and IRT phenotypes. In addition, the microarrays employ sequences of between 3 and 20 nucleotides around the triplet specific of the TEM enzyme, which are not random sequences but are derived from the TEM gene. These sequences are used to obtain the specific hybridization of the beta-lactamase gene as explained in the examples and as outlined in the description of the probe sequences given in table 2. The sequences specific for the TEM beta-lactamase of the capture molecules presented in figure 2 have a length from 18 to 27 nucleotides and include the given triplet in their sequence.

Furthermore, and contrary to the examiner's assertion (Advisory Action, pg. 3), the claimed invention involves simultaneously determining the genotype of the beta-lactam resistance. *See, e.g.* claim 1, preamble and step (iv). Applicants have amended the claims to further clarify this point.

Thus, the inventive methods and kits provide a practitioner, in a single assay, with a complete picture of a patient's status as to beta-lactam resistant microorganisms. Such assays represent a significant advancement in patient care that is neither taught or suggested by the prior art.

The examiner cites Lee for disclosing a micro-array for the detection of various beta-lactamase resistant genes. Blazquez is cited for teaching that amino acid replacement at seven residues of the TEM1 gene can alter resistance of microorganisms to specific antibiotics. Meanwhile, Chee (A) is cited for teaching a tilling array, and Sutcliffe is cited for disclosing the nucleotide sequence of the beta-lactamase gene. Osana is cited for teaching that class A and C beta-lactamases are serine dependent, that class B beta-lactamases are zinc-dependent and that some strains of the Enterobacteriaceae family are resistant to imipenem therapy. Chee (B) is cited for teaching that fragmentation improves uniformity and specificity of hybridization, while Routier is cited for teaching a method of fragmentation.

The cited materials, however, do not disclose or suggest a set of capture probes comprising the sequence $R^1$-(X)-$R^2$, which sequence represents a selected part of the sequence of a beta-lactamase gene among the TEM beta-lactamases exhibiting Extended Spectrum (ESBL) or Inhibitor Resistant (IRT) phenotype, wherein X represents a nucleotide triplet of table 1, and wherein $R^1$ and $R^2$ each have a length of from about 3 to 20 nucleotides specific for the TEM beta lactamase gene.

Similarly, the cited materials fail to disclose or suggest using sets of such capture probes in a method for detecting the presence of a beta-lactam resistant micro-organism in a biological sample and simultaneously determining the genotype of the beta-lactam resistance. Thus, no combination of the cited references presages the claimed invention.

Nor would one of ordinary skill in the art have combined the cited documents to reach the claimed invention with a reasonable expectation of success. The challenge of determining multiple possible mutations by array is that every part to be questioned has to be present in the amplified solution and they all have to be able to hybridize on their respective capture probes with discrimination between the wild and the mutated sequence to be large enough to be considered as positive or negative. The determination of a significant difference of hybridization of one nucleotide sequence on two capture probes differing by a single nucleotide resides is not trivial. Applicants have shown, however, that the present method permits a fast screening for antibiotic resistances and enables an immediate provision of a specially tailored antibiotic treatment with minimum delay, for example in less than one working day (e.g. page 15, par. 63). Such results enhance patient health while reducing costs. Applicants request, therefore, that the rejection be withdrawn.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16, 1.17 and 41.20, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

If any extensions of time are needed for timely acceptance of papers submitted herewith, applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date 21 November 2007 By _____

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